

LISTING AND AMENDMENT OF THE CLAIMS:

1. (Original) The use of an angiotensin derivative comprising at least one angiotensin peptide moiety coupled to a peptide carrier-binding moiety in the manufacture of a medicament for use in combatting diseases associated with the renin-angiotensin system.
2. (Original) The use as claimed in claim 1 wherein the angiotensin moiety comprises angiotensin I or angiotensin II or a functional equivalent of angiotensin I or angiotensin II.
3. (Previously presented) The use as claimed in claim 1 wherein the carrier binding moiety contains an amino acid residue having a reactive side chain.
4. (Previously presented) The use as claimed in claim 3 wherein the carrier binding moiety is a peptide extension at the N- or the C-terminus of an angiotensin peptide moiety.
5. (Previously presented) The use as claimed in claim 1 wherein the angiotensin derivative is of Formula I
$$((A)-X_n)_m-L_p-Y-[L_q(X_r-(A))_s]_t \quad (I)$$
wherein
 - A represents an angiotensin peptide moiety;
 - X represents an amino acid;
 - Y represents an amino acid having a side chain with a free -SH, -OH or -COOH group;
 - L represents an organic linker capable of binding a group $((A)-X_n)$ - at one or more sites, e.g. capable of binding up to 10 $(A)X_n$ moieties;
 - n and r are each = 0-20;
 - m and s are each ≥ 1 , e.g. 1 to 10, preferably 1, 2, 3 or 4; and
 - p, q and t are each 0 or 1;
 - wherein X may be attached at the N- or C-terminus of the angiotensin peptide moiety with the proviso that if $m \geq 2$, then $p=1$, or if $s \geq 2$, then $q=1$.

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6. (Original) The use as claimed in claim 5 wherein A is an angiotensin peptide.
7. (Previously presented) The use as claimed in claim 5 wherein L is a peptide chain.
8. (Previously presented) The use as claimed in claim 5 wherein n and r are each 0-10.
9. (Previously presented) The use as claimed in claim 5 wherein m and s are each <8.
10. (Previously presented) The use as claimed in claim 5 wherein X is an amino acid having no side chain or a hydrocarbyl side chain (preferably an alkyl, C₃₋₇, cycloalkyl or cycloalkenyl, C₃₋₇ cycloalkyl- or cycloalkenyl-alkyl, alkaryl, aralkyl or alkarylalkyl moiety in which each alkyl moiety may be saturated or unsaturated and contains up to 6 carbons and each aryl moiety is preferably a phenyl ring), particularly preferably an aliphatic side chain.
11. (Previously Presented) The use as claimed in claim 5 wherein X is glycine, alanine, β -alanine, valine, leucine or isoleucine.
12. (Previously presented) The use as claimed in claim 5 wherein the angiotensin derivative is selected from

| | |
|---|-------|
| (A)-X _n -Y | (II) |
| (A)-X _n -L-Y | (III) |
| ((A)-X _n) _m -L-Y | (IV) |
| (A)-X _n -L-Y-L-X _r -(A) | (V) |

wherein A, X, L, n and r are as hereinbefore defined and m \geq 2.

13. (Previously presented) The use as claimed in claim 1 wherein the angiotensin derivative is selected from

(A)-Gly Cys

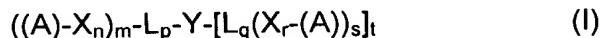
(A)-Cys
(A)-Tyr
N-acetyl-Cys-(A)
Tyr-(A)
N-acetyl-Cys-Gly-(A)
Cys – (A)
(A) – N-acetyl-Cys

where A is angiotensin I or II.

14. (Previously presented) The use as claimed in claim 1 wherein the angiotensin derivative elicits a cross-reactive immune response with angiotensin I, angiotensin II, and/or angiotensinogen molecules.
15. (Previously presented) The use as claimed in claim 1 wherein the angiotensin derivative is conjugated to a carrier.
16. (Original) The use as claimed in claim 15 wherein said carrier is a polypeptide.
17. (Original) The use as claimed in claim 16 wherein the carrier is selected from the purified protein derivative of tuberculin, tetanus toxiod, diphtheria toxiod, keyhole limpet haemocyanin or derivatives thereof.
18. (Previously presented) The use as claimed in claim 1 wherein said disease is congestive heart failure or hypertension.
19. (Original) The use as claimed in claim 18 for the modulation of blood pressure.
20. (Previously presented) A pharmaceutical composition comprising an angiotensin derivative as defined in claim 5, together with one or more pharmaceutically acceptable carriers or excipients.

21. (Previously presented) An angiotensin derivative as defined in claim 5 for use in therapy.

22. (Original) An angiotensin derivative of Formula I



wherein

A represents an angiotensin peptide moiety;

X represents an amino acid;

Y represents an amino acid having a side chain with a free -SH, -OH or -COOH group;

L represents an organic linker capable of binding a group ((A)-X_n)- at one or more sites, e.g. capable of binding up to 10 (A)X_n moieties;

n and r are each = 0-20;

m and s are each ≥ 1, e.g. 1 to 10, preferably 1, 2, 3 or 4; and

p, q and t are each 0 or 1;

wherein X may be attached at the N- or C-terminus of the angiotensin peptide moiety with the proviso that if m≥2, then p=1, or if s≥2, then q=1.

23. (Previously presented) An angiotensin derivative as claimed in claim 22 wherein L is a peptide chain.

24. (Previously presented) An angiotensin derivative as claimed in claim 22 wherein n and r are each 0-10.

25. (Previously presented) An angiotensin derivative as claimed in claim 22 wherein m and s are each ≤ 8.

26. (Previously presented) An angiotensin derivative as claimed in claim 22 wherein X is an amino acid having no side chain or a hydrocarbyl side chain (preferably an alkyl, C₃₋₇, cycloalkyl or cycloalkenyl, C₃₋₇ cycloalkyl- or cycloalkenyl-alkyl, alkaryl, aralkyl or alkarylalkyl moiety in which each alkyl moiety may be saturated or unsaturated and contains up to 6 carbons and each aryl moiety is preferably a phenyl ring), particularly preferably an aliphatic side chain.

Appl. No.: 10/470,997
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27. (Previously presented) An angiotensin as claimed in claim 22 wherein X is glycine, alanine, β -alanine, valine, leucine or isoleucine.

28. (Previously presented) An angiotensin derivative as claimed in claim 22 selected from

| | |
|---|-------|
| (A)-X _n -Y | (II) |
| (A)-X _n -L-Y | (III) |
| ((A)-X _n) _m -L-Y | (IV) |
| (A)-X _n -L-Y-L-X _r -(A) | (V) |

wherein A, X, L, n and r are as hereinbefore defined and m \geq 2.

29. (Previously presented) An angiotensin derivative as claimed in claim 22 selected from

N-acetyl-Cys-(A)
Tyr-(A)
N-acetyl-Cys-Gly-(A)
Cys – (A)

where A is angiotensin I.

30. (Previously presented) An angiotensin derivative as claimed in claim 22 which elicits a cross-reactive immune response with angiotensin I, angiotensin II, and/or angiotensinogen molecules.

31. (Previously presented) An angiotensin derivative as claimed in claim 22 conjugated to a carrier.

32. (Original) An angiotensin derivative as claimed in claim 31 wherein said carrier is a polypeptide.

33. (Original) An angiotensin derivative as claimed in claim 32 wherein the carrier is selected from the purified protein derivative of tuberculin, tetanus toxoid, diphtheria toxoid, keyhole limpet haemocyanin or derivatives thereof.

34. (Previously presented) A method of combatting conditions associated with activation of the renin-angiotensin system comprising administering an angiotensin derivative as defined in claim 5.

35. (Previously presented) A nucleic acid molecule coding for a linear angiotensin peptide derivative as claimed in claim 5, and nucleic acid molecules with sequences complementary thereto.

36. (Original) An expression vector comprising a nucleic acid molecule as claimed in claim 35.

37. (Original) A host organism transformed with the vector of claim 36.

38. (Previously presented) A method of combating conditions associated with the renin-angiotensin system comprising administering a nucleic acid molecule coding for a linear angiotensin peptide derivative as claimed in claim 1 or an expression vector comprising a nucleic acid molecule coding for any angiotensin peptide derivative.

39. (Currently amended) A polypeptide immunogen capable when conjugated to a carrier of inducing antibodies in an immunized subject, which antibodies recognize epitopes of angiotensin I, angiotensin II and/or angiotensinogen, said immunogen comprising an angiotensin derivative selected from the group consisting of:

- (A)-Gly-Cys (SEQ ID NO: 3);
- (A)-Cys (SEQ ID NO: 5);
- (A)-Tyr (SEQ ID NO: 6);
- N-acetyl-Cys-(A) (SEQ ID NO: 8);
- Tyr-(A) (SEQ ID NO: 7);
- N-acetyl-Cys-Gly-(A) (SEQ ID NO: 29);
- Cys-(A) (SEQ ID NO: 8); and

(A)-N-acetyl-Cys (SEQ ID NO: 31)
where A is angiotensin I (SEQ ID NO: 1).

40. (Original) An immunogen as claimed in claim 39 comprising said angiotensin derivative coupled to m-maleimidobenzoyl-N-hydroxysulphosuccinimide ester.

41. (currently amended) An immunogen as claimed in claim 39 wherein said angiotensin derivative is N-acetyl-Cys-(A) (SEQ ID NO: 8).

42. (Original) An immunogen as claimed in claim 39 wherein said angiotensin derivative is Tyr-(A) (SEQ ID NO: 7).

43. (currently amended). An immunogen as claimed in claim 39 wherein said angiotensin derivative is N-acetyl-Cys-Gly-(A) (SEQ ID NO: 29).

44. (Original) An immunogen as claimed in claim 39 wherein said angiotensin derivative is Cys-(A) (SEQ ID NO: 8).